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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,961	MOCK, MICHELE	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *8-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-7 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/8/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-7, in the paper filed 10/31/03 is acknowledged. The traversal is on the ground(s) that Group I is directed to immunogenic compositions or vaccines and Group IV is directed to antigenic preparation yet the Examiner provides no further explanation of why the Groups are separated. The composition of Group I comprises protective antigen and a preparation of killed spores from a mutant bacterium. The composition of claim 10 comprises one or more isolated exoantigens. These compositions contain entirely different components and therefore have completely different special technical features. Group II is directed to the RPLC2 strain. This strain is not required in Group I. The composition of Group I is completely different from the RPLC2 strain. Applicants mention that claim 5 recites spores derived from the RPLC2 strain; however, this strain is not required in claims 1-4 and 7 and even claims 5 and 6 are not claiming the strain itself. The special technical feature of Group I is not the RPLC2 strain, but is the composition comprising protective antigen and killed spores.

Claims 8-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-7 and new claims 12-15 are currently under examination.

The requirement is still deemed proper and is therefore made **FINAL**.

Specification

2. The disclosure is objected to because of the following informalities:

In the 'Brief Description of the Drawings' on page 9, line 11, 'figure 2' should be changed to 'figure 2A and 2B'.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-7 and 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3 recite that the compositions comprise protective antigen, but do not indicate that the protective antigen is isolated. Accordingly, the claims read on protective antigen in a strain of *B.anthracis* which has not been isolated. This does not appear to be what Applicants intend to claim. The claims should be amended to recite that the protective antigen in the composition is isolated. The claim should also recite that the protective antigen is from *B.anthracis* since the term 'protective antigen', on its own, could encompass many different antigens and is not limited to protective antigen from *Bacillus anthracis*.

Claims 1 and 3 are vague and indefinite due to the recitation of "mutations in at least one gene encoding a protein responsible for a toxic effect in *B.anthracis*'. It is unclear what is encompassed by this language. The specification teaches that protective antigen, lethal factor, and edematogenic factor are toxins responsible for a toxic effect. Only mutant strains carrying mutations for one of these toxins are taught. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. The name of the toxins, i.e., protective antigen lethal factor, and edematogenic factor, should be recited in the claim.

Claims 1 and 3 are vague and indefinite due to the recitation of the phrase 'optionally purified'. It is generally viewed that if an ingredient or method step is optional, it does not belong in the claim. Further, since the intended use of the composition is as an immunogen, it would seem that the components would need to be purified.

Claim 2 is vague and indefinite due to the phrase "capable of" because having the capability is not the same thing as actually performing the function. A positive recitation of the function is required.

Claims 4 and 12 are vague and indefinite for the phrase 'the lethal factor' and 'the edematogenic factor'. The word 'the' which proceeds the toxin name must be removed from the claim because there is insufficient antecedent basis for these limitations in the claim.

Claim 5-7 and 13-15 are vague and indefinite due to the term 'derived'. The term "derived" does not provide the character or properties from the source that are to be retained in the final product, e.g., paper is derived from wood but is very different from wood. The phrase "derived from" should be changed to "isolated from".

Claims 6 and 14 are vague and indefinite due to the recitation 'the recombinant protective antigens'. There is no antecedent basis for this phrase. Additionally, it is unclear which recombinant protective antigens the claim is referring to. It is suggested that the claim be amended to recite 'and recombinantly produced protective antigens'.

Claims 6 and 4 are also vague and indefinite for the phrase 'the purified protective antigens' in line 2. The word 'the' must be removed from the claims because the way it is currently written lacks antecedent basis.

Claim 7 is vague and indefinite due to the recitation of the term 'or vaccine composition'. Claim 7 does not depend from a vaccine claim. Claims 1 and 6, from which the claim depends, are drawn to immunogenic compositions. The phrase 'or vaccine composition' must be removed from the claim.

Claim Rejections - 35 USC § 112-Deposit Requirement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 5, 7, 13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the cell lines recited in the claims. Because it is not clear that the properties of these cell lines are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the best mode disclosed by the specification requires the use of the cell lines, a suitable deposit for patent purposes is required. Accordingly, filing of evidence of the reproducible production plasmids, one of ordinary skill in the art could be assured to the ability to practice the invention as claimed. Exact replication of the plasmids is an unpredictable event.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of the deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the

specification to recite the date of the deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

© the deposits will be maintained in a public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become non-viable or non-replicable.

In addition, a deposit of the biological material that is capable of self-replication either directly or indirectly must be viable at the time of the deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited

material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1)The name and address of the depository;

2)The name and address of the depositor;

3)The date of deposit;

4)The identity of the deposit and the accession number given by the depository;

5)The date of the viability test;

6)The procedures used to obtain a sample if the test is not done by the depository; and

7)A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 112-Enablement

7. Claims 1-7 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to "acellular immunogenic compositions or vaccines capable of inducing an immune response against *B.anthracis* infections, characterized in that it comprises: a protective antigen (PA), killed, optionally purified, spores obtained either from mutant strains of *B. anthracis* carrying one or more mutations chosen from mutations in at least one gene encoding a protein responsible for a toxic effect, in *B. anthracis*, or from mutant strains of *B. anthracis* lacking at least one of the pXOl and pXO2 plasmids, combined at least with a pharmaceutically acceptable vehicle'. Dependent claims recite that the spores may be derived from the Sterne 7702 strain, the RPLC strain and the RP42 strain. However, the instant specification only provides immunization results from experimentations carried out using protective antigen and killed spores derived from the Sterne 7702 strain. The Sterne 7702 strain carries only the plasmid pX01 which carries genes which encode the protective antigen (PA), lethal factor (LF) and the edematogenic factor (EF) and does not carry the pXO2 plasmid which carries the genes which synthesize the capsule. Accordingly, the Sterne 7702 strain is a toxigenic, non-encapsulated strain. The instant claims read on a much broader scope than what has been demonstrated to be effective in the instant specification. More

specifically, they read on vaccines and compositions which comprise killed spores derived from strains which do not carry the pX01 plasmid, strains which do not carry either the pX01 and pX02 plasmid and mutant strains which do not carry genes for one of the three toxins, i.e., PA, LF and EF. These strains are very different from the Sterne 7702 strain and the prior art has shown that they have a great deal of variation in the their immunogenic and protective effects. Pezard et al. (Infect. Immun. Apr.1995, 63(4): 1369-1372) teaches that animals immunized with strains which were deficient in the production of PA did not produce a good antibody response to EF or LF. In contrast, when LF or EF was produced by strains which also produce PA, a significant increase in the response against LF or EF was observed. The article by Pezard shows there is great variability in the immune response and the ability to protect against infection in various mutant strains, see Tables 1 and 2 on page 1371. Ivins et al. (Eur. J. Epidemiology. Mar. 1988. 4(1): 12-19) teaches that immunization with mutant strains carrying only the pX02 plasmid and not the pX01 plasmid (i.e., non-toxigenic, encapsulated strains) did not provide any protection, nor did double mutants which contained neither the pX01 or pX02 plasmids. Ivins teaches that strains which did not produce any toxin components were not protective. Ivins et al (Infect. Immun. May 1986, 52(2):454-8) teaches that immunization with two non-toxigenic, encapsulated ($pX01^-$, $pX02^+$), Pasteur strains neither provided protection nor elicited titers to any of the toxin components. Ivins teaches that to immunize successfully against anthrax toxin or spore challenge, the strains of *B.anthracis* must produce the toxin components specified by the pX01 plasmid. The prior art has established that immunogenicity of *B.anthracis* mutant strains

varies greatly. The spores derived from these strains would therefore vary in the same manner. Accordingly, the specification only enables vaccines and immunogenic compositions which utilize killed spores from a non-encapsulated, toxigenic *B.anthracis* strain, i.e., a strain which carries the pX01 plasmid and lacks the pX02 plasmids. Additional evidences may be submitted to support additional scopes.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-3, 5-7 and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Kraevets et al. Microbiology Res. Inst. July 1998, Derwent abstract only).

Kraevets et al teach a mixed anthrax vaccine comprising living spores of a non-encapsulated strain of *B.anthracis* and a protective antigen of *B.anthracis*. *B.anthracis* is normally encapsulated. It is well known in the art that the pX02 plasmid is responsible for capsule production. Accordingly, the strain used to obtain the live spores in the Kraevets reference is encompassed by the language of the instant claims. Although the reference does not specifically recite that the spores came from one of the specific strains recited in instant claims 5, 7, 13 and 15, it was well known in the prior art at the time the invention was made that the Sterne 7702 strain is a nonencapsulated strain which carries only the pXO1 plasmid and not the pXO2

plasmid. Additionally, a strain without a capsule would be considered to be a mutant 'lacking a gene encoding a protein responsible for a toxic effect'. Use of the specific strains recited in the dependent claims does not appear to be a critical factor as long as the strain meets the criteria set forth in independent claims 1 and 3. A different strain with the same properties would have been an obvious functional equivalent.

However, Kravets does not disclose that the spores to be used in the vaccine can be killed. It was well known in the prior art at the time the invention was made that live spores from *B.anthracis* had high lethality and were a risk to work with in the laboratory. Live spore vaccines were only approved for veterinary use and not human use. Killed anthrax vaccines were well known in the prior art to be safe and efficacious when used in humans. Absent a showing of new or unobvious results, it would have been obvious to substitute killed spores of a non-encapsulated strain of *B.anthracis* in place of the live spores taught by Kraevts because doing so would allow for easier manipulation in the laboratory and a reduced incidence of lethality in the host to be vaccinated.

10. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 872-9306 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 272-0858. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 272-0864.

Jennifer Graser
Primary Examiner
Art Unit 1645

2/9/04